



## microphthalmia with linear skin defects syndrome

Microphthalmia with linear skin defects syndrome is a disorder that mainly affects females. In people with this condition, one or both eyes may be very small or poorly developed (microphthalmia). Affected individuals also typically have unusual linear skin markings on the head and neck. These markings follow the paths along which cells migrate as the skin develops before birth (lines of Blaschko). The skin defects generally improve over time and leave variable degrees of scarring.

The signs and symptoms of microphthalmia with linear skin defects syndrome vary widely, even among affected individuals within the same family. In addition to the characteristic eye problems and skin markings, this condition can cause abnormalities in the brain, heart, and genitourinary system. A hole in the muscle that separates the abdomen from the chest cavity (the diaphragm), which is called a diaphragmatic hernia, may occur in people with this disorder. Affected individuals may also have short stature and fingernails and toenails that do not grow normally (nail dystrophy).

### Frequency

The prevalence of microphthalmia with linear skin defects syndrome is unknown. More than 50 affected individuals have been identified.

### Genetic Changes

Mutations in the *HCCS* gene or a deletion of genetic material that includes the *HCCS* gene cause microphthalmia with linear skin defects syndrome. The *HCCS* gene carries instructions for producing an enzyme called holocytochrome c-type synthase. This enzyme is active in many tissues of the body and is found in the mitochondria, the energy-producing centers within cells.

Within the mitochondria, the holocytochrome c-type synthase enzyme helps produce a molecule called cytochrome c. Cytochrome c is involved in a process called oxidative phosphorylation, by which mitochondria generate adenosine triphosphate (ATP), the cell's main energy source. It also plays a role in the self-destruction of cells (apoptosis).

*HCCS* gene mutations result in a holocytochrome c-type synthase enzyme that cannot perform its function. A deletion of genetic material that includes the *HCCS* gene prevents the production of the enzyme. A lack of functional holocytochrome c-type synthase enzyme can damage cells by impairing their ability to generate energy. In addition, without the holocytochrome c-type synthase enzyme, the damaged cells may not be able to undergo apoptosis. These cells may instead die in a process called necrosis that causes inflammation and damages neighboring cells. During early

development this spreading cell damage may lead to the eye abnormalities and other signs and symptoms of microphthalmia with linear skin defects syndrome.

## **Inheritance Pattern**

This condition is inherited in an X-linked dominant pattern. The gene associated with this condition is located on the X chromosome, which is one of the two sex chromosomes. In females (who have two X chromosomes), a mutation in one of the two copies of the gene in each cell is sufficient to cause the disorder. Some cells produce a normal amount of the holocytochrome c-type synthase enzyme and other cells produce none. The resulting overall reduction in the amount of this enzyme leads to the signs and symptoms of microphthalmia with linear skin defects syndrome.

In males (who have only one X chromosome), mutations result in a total loss of the holocytochrome c-type synthase enzyme. A lack of this enzyme appears to be lethal very early in development, so almost no males are born with microphthalmia with linear skin defects syndrome. A few affected individuals with male appearance but who have two X chromosomes have been identified.

Most cases of microphthalmia with linear skin defects syndrome occur in people with no history of the disorder in their family. These cases usually result from the deletion of a segment of the X chromosome during the formation of reproductive cells (eggs and sperm) or in early fetal development. They may also result from a new mutation in the *HCCS* gene.

## **Other Names for This Condition**

- MCOPS7
- microphthalmia syndromic 7
- microphthalmia with linear skin lesions syndrome
- microphthalmia, dermal aplasia, and sclerocornea
- microphthalmia, syndromic 7
- MIDAS syndrome
- MLS syndrome
- syndromic microphthalmia-7

## **Diagnosis & Management**

### Genetic Testing

- Genetic Testing Registry: Linear skin defects with multiple congenital anomalies 1 <https://www.ncbi.nlm.nih.gov/gtr/conditions/C0796070/>

### Other Diagnosis and Management Resources

- GeneReview: Microphthalmia with Linear Skin Defects Syndrome  
<https://www.ncbi.nlm.nih.gov/books/NBK7041>

### General Information from MedlinePlus

- Diagnostic Tests  
<https://medlineplus.gov/diagnostictests.html>
- Drug Therapy  
<https://medlineplus.gov/drugtherapy.html>
- Genetic Counseling  
<https://medlineplus.gov/geneticcounseling.html>
- Palliative Care  
<https://medlineplus.gov/palliativecare.html>
- Surgery and Rehabilitation  
<https://medlineplus.gov/surgeryandrehabilitation.html>

## **Additional Information & Resources**

### MedlinePlus

- Health Topic: Eye Diseases  
<https://medlineplus.gov/eyediseases.html>
- Health Topic: Skin Conditions  
<https://medlineplus.gov/skinconditions.html>

### Genetic and Rare Diseases Information Center

- Microphthalmia syndromic 7  
<https://rarediseases.info.nih.gov/diseases/3659/microphthalmia-syndromic-7>

### Additional NIH Resources

- National Eye Institute: Anophthalmia and Microphthalmia  
<https://nei.nih.gov/health/anoph/>

### Educational Resources

- Disease InfoSearch: Microphthalmia syndromic 7  
<http://www.diseaseinfosearch.org/Microphthalmia+syndromic+7/4791>
- Orphanet: Microphthalmia with linear skin defects syndrome  
[http://www.orpha.net/consor/cgi-bin/OC\\_Exp.php?Lng=EN&Expert=2556](http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=2556)

## Patient Support and Advocacy Resources

- American Foundation for the Blind  
<http://www.afb.org/>
- Foundation Fighting Blindness  
<http://www.blindness.org/>

## GeneReviews

- Microphthalmia with Linear Skin Defects Syndrome  
<https://www.ncbi.nlm.nih.gov/books/NBK7041>

## ClinicalTrials.gov

- ClinicalTrials.gov  
<https://clinicaltrials.gov/ct2/results?cond=%22Microphthalmos%22+OR+%22microphthalmia+with+linear+skin+defects+syndrome%22>

## Scientific Articles on PubMed

- PubMed  
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28midas+syndrome%5BTIAB%5D%29+OR+%28mls+syndrome%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D>

## OMIM

- LINEAR SKIN DEFECTS WITH MULTIPLE CONGENITAL ANOMALIES 1  
<http://omim.org/entry/309801>

## **Sources for This Summary**

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